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Microemboli detected by transcranial Doppler monitoring in patients during carotid angioplasty *versus* carotid endarterectomy

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Microemboli, as detected by transcranial Doppler monitoring, have been shown to be a potential cause of strokes after carotid endarterectomy. We retrospectively reviewed 105 patients who underwent transcranial Doppler monitoring during 112 procedures for the treatment of 115 carotid bifurcation stenoses: 40 by percutaneous angioplasty with stenting and 75 by carotid endarterectomy. In PTAS procedures (n = 40), there was a mean of 74.0 emboli per stenosis (range 0–398, $P = 0.0001$) with 4 neurologic events per patient ($P = 0.08$). In CEA procedures ($n = 76$), there was a mean of 8.8. emboli per stenosis (range 0–102, $P = 0.0001$) with 1 neurologic event per patient ($P = 0.08$). The post-procedural neurological events in the percutaneous angioplasty with stenting population included two strokes (5.6%) and two transient ischemia attacks (5.6%). Microemboli for each of these cases totalled 133, 17, 29 and 47 (with one shower), respectively. One postoperative carotid endarterectomy patient was noted to have a stroke (1.4%), with 48 microemboli noted during that procedure. The mean emboli rate for percutaneous angioplasty with stenting patients with neurological events was 59.0: without complications it was 85.1. The mean emboli rate for carotid endarterectomy patients without complications was 8.3. Three percutaneous angioplasty with stenting patients had no emboli (7.5%), whereas 29 carotid endarterectomy patients had no emboli (38.7%). Conclusion: The percutaneous angioplasty with stenting procedure is associated with more than eight times the rate of microemboli seen during carotid endarterectomy when evaluated with transcranial Doppler monitoring. Larger patient groups are needed to determine if this greater embolization rate has an associated risk of higher morbidity or mortality.
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Carotid endarterectomy has become established as the treatment of choice for symptomatic and asymptomatic patients with high-grade carotid stenosis [1, 2]. Despite a well-established record as an intensely scrutinized operation, other modalities of treatment have been explored. More recently, endovascular techniques have been applied to the treatment of carotid stenosis with the objectives of reducing morbidity, lowering costs, avoiding general anesthesia and improving long-term vascular pat-

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ency. With Institutional Review Board approval, percutaneous angioplasty and stent placement for the treatment of carotid bifurcation stenoses is under investigation at our institution. A comparison of this technique of percutaneous angioplasty with stenting with the surgical results at the authors' institution has been previously reported [3].

Transcranial Doppler has been used as a monitoring tool during carotid endarterectomy to determine hemodynamic changes in the middle cerebral artery during carotid endarterectomy and to identify high-intensity transients that are thought to be air or particulate embolic material that is insonated in the ipsilateral middle cerebral artery [4–10]. This transcranial Doppler blood flow velocity is considered in the decision for shunt placement during the carotid occlusion portion of the carotid endarterectomy surgical procedure. The high-intensity transients data can be used to modify the surgical technique to avoid further embolization [10]. The embolic potential for arterial embolization during percutaneous angioplasty with stenting has created some concern about the technique and has led to hesitancy of its use among carotid physicians. Other investigators, Markus *et al.* [11], have questioned the clinical significance of the emboli counts. We undertook this study to compare microemboli detected by transcranial Doppler monitoring during both percutaneous angioplasty with stenting and carotid endarterectomy, and to identify the clinical outcomes of each group of patients.

Methods

A review was performed of all patients who underwent elective treatment for carotid stenosis by either carotid endarterectomy or percutaneous carotid angioplasty with stenting, and who were monitored by transcranial Doppler from August 1994 through to November 1995 at the University of Alabama at Birmingham Hospital. Intraoperative transcranial Doppler monitoring was done routinely in this carotid endarterectomy population without special patient selection. Intra-procedural transcranial Doppler monitoring was used for a brief time during the evaluation of all percutaneous angioplasty with stenting procedures, but was later discontinued because of inconclusive clinical information. Monitoring was not routinely done post-procedure. Clinic notes, hospital charts and computerized registries were retrospectively analyzed for patient characteristics, type of procedure, indications for the procedure, plaque morphology, neurological and non-neurological complications, number and timing of microemboli as detected by transcranial Doppler monitoring.

Patient characteristics reviewed were sex, age and pre-existing co-morbidities, including coronary artery disease, hypertension and diabetes melitis. The indications for the procedure were divided into three groups: (i) asymptomatic (including global, non-lateralizing symptoms), (ii) transient ischemic attack, including amaurosis fugax, and (iii) cerebrovascular accident. Transient ischemic attacks resolved within 24 hours, whereas strokes were classified as lasting longer than 24 hours. The neurological event must have occurred within 4 months prior to surgery in order to be considered an indication for the procedure [1]. Plaque morphology was determined by reviewing carotid Doppler reports, angiogram reports and operative notes, and was classified as ulcerative or non-ulcerative in a non-blinded fashion. Doppler ultrasound criteria for ulceration was defined as an obvious defect in the arterial lumen seen in β-mode. Angiographic ulceration was defined as an arterial defect from baseline as noted by the radiologist or surgeon. Degrees of stenosis were considered significant ($>$ 60%) in both groups but were measured by two different modalities between the carotid endarterectomy and percutaneous angioplasty with stenting groups, and were not compared. Neurological complications were defined as either transient ischemic attacks or strokes.

Transcranial Doppler monitoring was performed using either a Medasonics (Model CDS, Medasonics, Inc., Fremont, CA) or an Eden Medical Electronics (EME, Model TC2000S, Nicolet, Inc., Memphis, TN) probe secured to the patient's head over the temporal bone above the zygomatic arch. In an unblinded fashion, high-intensity transient signals, which indicated microemboli, were identified from Doppler spectrae stored on a hard disk, according to the criteria given by the Consensus Committee of the Ninth International Cerebral Hemodynamic Symposium [12]. A shower of microemboli was considered to be 10 microemboli for statistical purposes. Timing of microemboli during percutaneous angioplasty with stenting was divided into three groups: (i) during catheter manipulation, (ii) during balloon inflation, and (iii) during balloon deflation. Timing of microemboli during carotid endarterectomy was divided into two groups: (i) before reperfusion of the carotid vessels (during dissection and clamping), and (ii) after reperfusion of the carotid vessels.

Percutaneous angioplasty with stenting was accomplished using a coaxial catheterization technique. After percutaneous femoral access was obtained, guiding catheters were positioned just proximal to the bifurcation to image the stenosis before an appropriately-sized balloon and stent wire were selected. Stenoses were crossed with a guidewire and pre-dilated with a balloon. All patients in this series received at least one stent dilated with balloon inflation at pressures of 10 to 16 atmospheres.

Carotid endarterectomy was performed using different surgical techniques by three different surgeons. Either regional anesthesia, balanced general anesthesia, or general anesthesia with EEG burst suppression produced by etomidate administration were used. EEG and transcranial Doppler monitoring were employed in all cases. Dacron patch angioplasty was used in cases where the operating surgeon felt the native vessel caliber was not sufficient.

Statistics between any two groups, for non-parametric data, used the Mann–Whitney rank sum test. For three groups, a one-way ANOVA with Dunn's method of comparison was used. Proportional data were analyzed using a z-test with Yates correction for continuity. All statistical analysis was performed on SigmaStat computer software (Jandel Corporation). A P-value of < 0.05 was considered statistically significant.

Results

From 16 March 1994 to 15 November 1995, 105 of 273 patients (38.5%) underwent transcranial Doppler monitoring during 112 procedures for the treatment of 115 carotid bifurcation stenoses at University Hospital. Percutaneous angioplasty with stenting was performed on 36 patients who underwent 37 procedures for 40 stenoses. Carotid endarterectomy was performed on 69 patients who underwent 75 procedures for 75 stenoses. Eighty-four patients were men (80.0%). The mean age of all patients was 67.2, range 41–85 years. There were no statistically significant differences in pre-existing co-morbidities for each procedural population, and these are listed in *Table 1*. Ulcerations were noted in 31 stenoses (27.0%): eight in percutaneous angioplasty with stenting stenoses (20.0%) and 23 in carotid endarterectomy stenoses (30.7%).

The mean number of microemboli during percutaneous angioplasty with stenting was 74.0 (median 39.5, range 0–398), whereas the mean number of microemboli during carotid endarterectomy was 8.8 (median 3.0, range 0–102, $P = 0.0001$). Three patients with percutaneous angioplasty with stenting had no emboli (7.5% of treated stenoses), whereas 29 carotid endarterectomy patients had no emboli (38.7%). The number of microemboli produced varied between procedure and plaque morphology as seen in *Table 2*. Non-ulcerative plaques produced a significantly greater number of microemboli than did ulcerative plaques ($P = 0.007$). The number of microemboli produced also varied during different procedural stages as noted in *Table 3*. The number of carotid endarterectomy microemboli noted after reperfusion was significantly greater than the number noted before reperfusion ($P = 0.0001$). The number of percutaneous angioplasty with stenting microemboli noted during catheter manipulation or balloon deflation was significantly greater than the number noted during balloon inflation.

Neurological complications occurred in four patients with percutaneous angioplasty with stenting (11.1%), and included two transient ischemic attacks, two cerebrovascular accidents and no deaths. All patients with percutaneous angioplasty with stenting had completion angiography that showed a patent stent and internal carotid artery. Two patients had monoparesis that persisted > 24 hours, one had monoparesis that resolved at 24 hours, and another had recurrent amaurosis evident after completion of the procedure. Neurological complications occurred in one carotid endarterectomy patient (1.4%) who awakened from general anesthesia with a hemiparesis. This patient was re-explored and an intraoperative arteriogram confirmed a patent carotid artery. The difference in combined neurological morbidity was not statistically significant ($P = 0.08$) (*Table 4*). The mean number of microemboli for all patients with neurological complications was 56.8, and for those without

Table 1 Patient characteristics

	PTAS	CEA	P-value
Patients	36	69	
Procedures	37	75	
Stenoses	40	75	
Mean age	67.0	67.3	0.79
Age range	44–85	41–83	
Male	32 (88.9%)	52 (75.4%)	0.17
CAD	23 (63.9%)	34 (49.3%)	0.22
Hypertension	21 (58.3%)	47 (68.1%)	0.43
Diabetes	10 (27.8%)	16 (23.2%)	0.78
Indications:	40	75	
Asymptomatic	29 (72.5%)	52 (69.3%)	0.89
TIA	9 (22.5%)	17 (22.7%)	0.83
CVA	2 (5.0%)	6 (8.0%)	0.83

CAD, coronary artery disease; TIA, transient ischemic attack; CVA, cardiovascular aneurysm

Table 2 Mean number of microemboli per stenosis (± s.e.)

	PTAS ($n = 40$)	CEA ($n = 75$)	Total ($n = 115$)
Asymptomatic	60.1 ± 11.9	8.9 ± 1.7	27.2 ± 5.1
TIA	115.1 ± 48.5	11.2 ± 6.3	47.2 ± 19.4
CVA	90.5 ± 18.5	1.3 ± 0.8	23.6 ± 15.0
P-value	0.40	0.12	0.52
Ulcer (PTAS = 8) (CEA = 23)	85.0 ± 36.1	4.0 ± 1.9	24.9 ± 11.1
No ulcer (PTAS = 32) (CEA = 52)	71.2 ± 15.3	10.9 ± 2.4	33.9 ± 6.8
P-value	0.723	0.053	0.007

PTAS, percutaneous angioplasty and stent placement; CEA, carotid endarterectomy; TIA, transient ischemic attack; CVA, cardiovascular aneurysm

Table 3 Mean number of microemboli per procedure (± s.e.)

CEA	Before reperfusion	After reperfusion		*P*-value
	1.6 ± 0.7	7.2 ± 1.4		0.0001
PTAS	Catheter manipulation	Balloon inflation	Balloon deflation	*P*-value
	35.0 ± 10.2	10.2 ± 2.5	30.5 ± 5.2	< 0.05*

PTAS, percutaneous angioplasty and stent placement; CEA, carotid endarterectomy

*$P < 0.05$ for catheter manipulation or balloon deflation when compared with balloon inflation

Table 4 Neurological complications (within 30 days)

	Indication	Ulcerative plaque	No. of emboli	C/I/D/O[a]	Neurologic event
PTAS	Asymptomatic	No	133	34/0/19/80	CVA
	Asymptomatic	No	17	3/1/3/10	CVA
	Asymptomatic	No	57	0/28/29/0	TIA
	TIA	No	29	7/7/15/0	TIA
				B/A[b]	
CEA	Asymptomatic	No	48	41/7	CVA

[a] (C/I/D/O). Catheter manipulation/balloon inflation/balloon deflation/other

[b] (B/A). Before reperfusion/after reperfusion

PTAS, percutaneous angioplasty and stent placement; CEA, carotid endarterectomy; TIA, transient ischemic attack; CVA, cardiovascular aneurysm

neurological complications it was 31.2 ($P = 0.02$). Patients with percutaneous angioplasty with stenting, with neurological complications, had a mean microembolic number of 59.0, and those without complications had 85.1. The carotid endarterectomy patient with neurological complications had 48 microemboli (the mean rate for carotid endarterectomy patients was 8.8, as noted above; carotid endarterectomy patients without neurological complications had a mean number of 8.3). The patient who had a cerebrovascular accident had the highest number (41) of microemboli identified before carotid clamping (*Figure 1*).

Discussion

Carotid balloon angioplasty with or without stent placement has been suggested as an alternative to endarterectomy in the treatment of high-grade stenosis. Our patient series provides a retrospective analysis of the differences in these two techniques, as can be established by transcranial Doppler monitoring. We compared the two treatment modalities with regards to emboli rates and subsequent post-procedure neurological changes.

Transcranial Doppler monitoring has become more common for evaluating patients with carotid

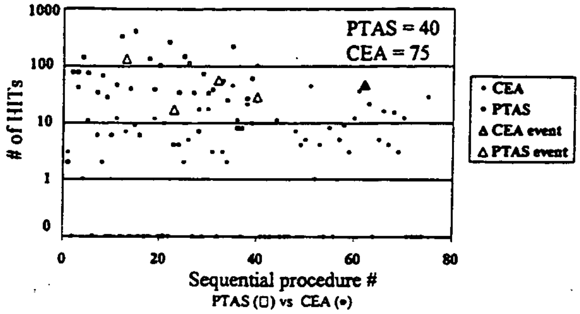

Figure 1 Mean total number of microemboli produced by each stenosis for all each individual procedures with neurological events highlighted. Procedures that led to neurological events are emphasized

stenosis. Continuous intraoperative transcranial Doppler monitoring provides hemodynamic information about the velocity of blood flow in the ipsilateral middle cerebral artery, that aids in the intraoperative decision about shunt placement during carotid endarterectomy, verification of shunt function, and restoration of blood flow following release of the cross-clamp [16]. We have also found that most high-intensity transients that occur during the procedure are identified following re-perfusion of the brain after the endarterectomy is completed. These data have led to some modification of our surgical technique to reduce embolic risk in the operation [10]. The exact nature of these emboli is not known. The distinction between particulate matter and air emboli is a topic of current investigation [8, 17, 18]. The emboli have not directly correlated with clinical neurological deficits in our series. However, other authors have identified a higher number of clinical neurological deficits and radiographically silent defects when the number of emboli is > 10 [4, 5].

This series demonstrates a clear and definite difference between the number of emboli produced between percutaneous angioplasty with stenting and carotid endarterectomy, as identified by transcranial Doppler monitoring. When considering the different mechanisms that these modalities employ for treatment of the stenosis, one would expect a different embolization risk. However, this small series does not identify a statistically significant difference between the neurological deficits in each group, only a trend. When examining the percutaneous angioplasty group with the stenting group, only four patients manifested neurological changes after the procedure, and these symptoms had resolved in two of these patients within 24 hours. The rate of embolization was not found to be excessive (17, 47 (with one shower), 133 and 29) when compared with the percutaneous angioplasty with stenting population as a whole. However, all of these would be considered high when compared with surgical embolization rates. Interestingly, eight patients with percutaneous angioplasty with stenting and one carotid endarterectomy patient had > 100 emboli, but had no clinically detectable neurological deficit.

Our series represents a small group of patients with a marginally different stroke rate. The 36 patients with percutaneous angioplasty with stenting had a 5.6% stroke rate, and the 69 carotid endarterectomy patients had a 1.4% stroke rate. Both of these rates are within the accepted range of the American Heart Association Consensus Council on stroke prevention and carotid endarterectomy [19]. However, this series does not represent a definitive statement on the stroke rates between these two groups. Instead, attention should be directed to a more definitive series of comparison groups at the authors' institution [19], which defined a stroke rate of 9–10% in patients with percutaneous angioplasty with stenting when they were evaluated as an aggregate group [3].

During the course of this review of percutaneous angioplasty with stenting, an appropriate group was sought on whom to apply this technique. Transcranial Doppler monitoring offers another way to identify the differences in the two treatment modalities of percutaneous angioplasty with stenting and carotid endarterectomy. We further subdivided these groups of patients to identify a group that might be at less embolic risk with percutaneous angioplasty with stenting. Non-ulcerative lesions had a higher embolization rate in carotid endarterectomy patients, although not in percutaneous angioplasty with stenting patients. This phenomenon seems contrary to the clinical concern that ulcerative lesions have a higher embolic rate. It may suggest that ulcerative lesions have completed their embolic 'release'. This suggests that patients with transient ischemic attacks may have more active embolic lesions than asymptomatic patients.

More recently, there has been a suggestion that air and particulate matter can be distinguished by transcranial Doppler monitoring [7, 17]. In the carotid endarterectomy patients, there was a significantly higher embolization rate after reperfusion of the middle cerebral artery compared to the amount before clamping or during carotid dissection. Many of these post-reperfusion microemboli are thought to be small air bubbles that were not completely evacuated from the carotid bulb. The majority of emboli in patients with percutaneous angioplasty with stenting occurred during initial catheter manipulation and carotid balloon deflation. While these emboli during catheter manipulation may represent air that is introduced from the catheter system during exchange, particulate matter is a more likely possibility.

Conclusions

Based upon emboli data derived from continuous transcranial Doppler monitoring, percutaneous angioplasty with stenting is associated with a higher embolic risk rate than carotid endarterectomy when used for the treatment of carotid stenosis. Clinical differences were not statistically significant, but a higher neurological complication rate can be expected to be associated with a higher rate of high-intensity transients.

References

1. North American Symptomatic Carotid Endarterectomy Trial Collaborators, Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *New England Journal of Medicine*, 1991, 325, 445–452.
2. Executive Committe for the Asymptomatic Carotid Atherosclerosis Study, Endarterectomy for asymptomatic carotid artery stenosis. *Journal of the American Medical Association*, 1995, 273, 1421–1428.
3. Jordan, W. D., Schroeder, P. T., Fisher, W. S. and McDowell, H. A., A comparison of angioplasty with stenting *versus* endarterectomy for the treatment of carotid artery stenosis. *Annals of Vascular Surgery*, 1997, 11, 2–8.
4. Ackerstaff, R. G. A., Jansen, C., Moll, F. L. *et al.*, The significance of microemboli detection by means of transcranial Doppler ultrasonography monitoring in carotid endarterectomy. *Journal of Vascular Surgery*, 1995, 21, 963–969.
5. Gaunt, M. E., Martin, P. J., Smith, J. L. *et al.*, Clinical relevance of intraoperative embolization detected by transcranial Doppler ultrasonography during carotid endarterectomy: a prospective study of 100 patients. *British Journal of Surgery*, 1994, 81, 1435–1439.
6. Van Zuilen, E. V., Moll, F. L., Vermeulen, F. E. E. *et al.*, Detection of cerebral microemboli by means of transcranial Doppler monitoring before and after carotid endarterectomy. *Stroke*, 1995, 26, 210–213.
7. Spencer, M. P., Thomas, G. I., Nicholls, S. C. and Sauvage, L. R., Detection of middle cerebral artery emboli during carotid endarterectomy using transcranial Doppler ultrasonography. *Stroke*, 1990, 21, 415–423.
8. Babikian, V. L., Hyde, C., Pochay, V. and Winter, M. R., Clinical correlates of high-intensity transient signals detected on transcranial Doppler sonography in patients with cerebrovascular disease. *Stroke*, 1994, 25, 1570–1573.
9. Jansen, C., Ramos, L. M. P., Van Heesewijk, J. P. M. *et al.*, *Impact of microembolism and hemodynamic changes in the brain during carotid endarterectomy. Stroke*, 1994, 25, 992–997.
10. McDowell, H. A., Gross, G. M. and Halsey, J. H., Carotid endarterectomy monitored with transcranial Doppler. *Annals of Surgery*, 1992, 215, 515–519.
11. Markus, H. S., Clifton, A., Buckenham, T. and Brown, M. M., Carotid angioplasty: detection of embolic signals during and after the procedure. *Stroke*, 1994, 25, 2403–2406.
12. Consensus Committee of the Ninth International Cerebral Hemodynamic Symposium, Basic identification criteria of Doppler microembolic signals. *Stroke*, 1995, 26, 1123.
13. Doblar, D. D., Plyushcheva, N. P., Bailey, C. *et al.*, TCD velocity with carotid occlusion: correlation with collateral circulation on angiography. *Journal of Neurosurgical Anesthesiology*, 1995, 8(4), 334.
14. Plyushcheva, N., Doblar, D. D., McDowell, H. and Jordan, W., Regional oxygen saturation (RSO2), TCD velocity (FV), and EEG after crossclamping during carotid endarterectomy. *Journal of Neurosurgical Anesthesiology*, 1995, 7, 322.
15. Plyuscheva, N., Doblar, D. D., Yadav, J. *et al.*, Embolism detection during carotid angioplasty using transcranial Doppler ultrasound. *Circulation*, 1995, 92, 3481.
16. Doblar, D. D., Frenette, L., Lim, Y. C. and Gross, G., Immediate detection of carotid arterial thrombosis by transcranial Doppler monitoring. *Anesthesiology*, 1994, 80, 209–212.
17. Russell, D., Madden, K. P., Clark, W. M. *et al.*, Detection of arterial emboli using Doppler ultrasound in rabbits. *Stroke*, 1991, 22, 253–258.
18. Kessler, C., Kelly, A. B., Suggs, W. D. *et al.*, Induction of transient neurological dysfunction in baboons by platelet microemboli. *Stroke*, 1992, 23, 697–702.
19. Ad Hoc Committee, American Heart Association, Guidelines for carotid endarterectomy: a multidisciplinary consensus statement from the Ad Hoc Committee, American Heart Association. *Stroke*, 1995, 26, 188–201.

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